

**REMARKS**

Reconsideration of this application is respectfully requested.

Claims 1-4 and 6-13 were pending in this application. By way of this amendment, claims 1-4 and 6-10 have been canceled without prejudice or disclaimer, and new claims 14-29 have been added. Accordingly, claims 11-29 will be pending in the instant application upon entry of this amendment. Support for the new claims may be found in the specification and claims as originally filed. No new matter has been added. Applicants would like to inform the Examiner that the corresponding European application serial no. 98 955 312.8 has been allowed.

The issues raised by the Examiner in the Office Action are summarized and addressed below.

**Rejection Under 35 U.S.C. §102(b) or 35 U.S.C. § 103(a) in view of Lamothe et al.**

The Examiner has rejected claims 1-4 and 6-13 under 35 U.S.C. §102(b) as being anticipated by Lamothe et al. (U.S. Patent No. 5,518,733), or, in the alternative, as being unpatentable over Lamonthe et al. under 35 U.S.C. §103(a). The Examiner contends that Lamothe et al. disclose a composition useful for the development of beneficial vaginal microflora and the preservation of acidic conditions comprising maltose and other fructo-oligosaccharides, a preserving agent having an antifungal action, and an acidic buffer which adjusts the pH of the composition to the 5 to 7 range. The Examiner states that Lamothe et al. further disclose a method for favoring bacilli development. The Examiner also contends that any differences between the claimed compositions and methods and the compositions and methods disclosed by Lamothe et al., are minor and would be obvious to one of ordinary skill in the art at the time of the invention.

Applicants respectfully traverse the foregoing rejection. With respect to claims 1-4 and 6-10, Applicants respectfully submit that these claims have been canceled, without prejudice or disclaimer, thereby rendering the rejection moot as it pertains to these claims.

With respect to claims 11-13 and new claims 14-29, Applicants respectfully submit that Lamothe et al. fail to teach or suggest each and every limitation of the claimed invention. Lamothe et al. disclose a method for favoring the development of endogenous flora on the skin and in the vagina comprising the application of oligosaccharides. The general formulas of saccharides disclosed in Lamothe et al. include hundreds of saccharides. However, not every saccharide has the same effect in promoting bacterial growth. As set forth in claim 1 of Lamothe et al., these saccharides promote the growth of many kinds of bacteria. In contrast, the present invention specifically claims the use of sucrose and/or maltose for promoting the selective growth of lactobacilli and for treating the specified diseases, *e.g.*, vaginitis, disturbance of the vaginal bacterial flora and bacterial vaginosis.

In addition, in the claims of this application, the diseases to be treated have been definitely limited to “a patient suffering from vaginitis, a disturbance of the vaginal bacterial flora or bacterial vaginosis, wherein said vaginitis, disturbance of the vaginal bacterial flora or bacterial vaginosis are accompanied with a reduction of the number of Gram-positive bacilli.” Lamothe et al. do not mention these diseases which may be treated using the methods of the present invention.

Lamothe et al. disclose that a cosmetic composition containing maltose can favor the development of some microorganisms on the skin or the vagina. Lamothe et al. also disclose that the composition may be in the form of a vaginal gel. However, the composition described in Lamothe et al. is not for treating diseases, *e.g.*, vaginitis, a disturbance of the vaginal bacterial flora, or bacterial vaginosis. It is for promoting the growth of many bacteria. In particular, it is mainly effective for promoting the growth of Gram-positive *cocci*, including *Micrococcus kristinae*, *Micrococcus sedentarius*, *Staphylococcus capitis*, etc. These bacteria, however, are not naturally occurring, beneficial vaginal bacteria. Please see Exhibits 1-3 from Applicants' previous Amendment and Response filed on December 3, 2004, which includes Abstracts from the following references which describe the vaginal species present in the vaginal flora and in vaginosis and vaginitis:

1) Rosenstein, I.J. et al., Bacterial vaginosis in pregnancy: distribution of bacterial species in different gram-stain categories of the vaginal flora. J Med Microbiol 1996 Aug; 45(2):120-6;

2) Hughes, V.L. et al., Microbiologic characteristics of Lactobacillus products used for colonization of the vagina. Obstet Gynecol 1990 Feb; 75(2):244-8; and

3) McLean, N.W. et al., Characterization and selection of a Lactobacillus species to re-colonize the vagina of women with re-current bacterial vaginosis. J Med Microbiol 2000 Jun; 49(6):543-52).

One of ordinary skill in the art would understand that if these bacteria proliferate in the vagina, they most probably would cause vaginal infection.

When one saccharide is administered vaginally, a massive increase in the number of bacteria other than Gram-positive bacilli may also occur and cause further harm to the patient. This would occur because there are dozens, even hundreds, of different kinds of bacteria in a patient having disturbed vaginal flora, vaginitis and vaginosis, while some of them remain unknown. It is clear that not all kinds of saccharides could be effective when administered vaginally to treat disturbance of vaginal flora, vaginitis or vaginosis. Prior to the present invention, without extensive and innovative studies, it was impossible for even the experts in the relevant art to predict what would happen after maltose or sucrose, or any other saccharide, is administered into the vagina. The general idea that saccharides can promote the growth of some kind of bacteria may sound reasonable; however, prior to the present invention, it failed to make any sense to vaginally administer saccharides to cure a disturbance of vaginal flora, vaginitis or vaginosis.

The present invention, however, is directed to treating vaginal diseases characterized by a reduction of Gram-positive bacilli, *i.e.*, lactobacilli, via promoting selective growth of Gram-positive bacilli in the vagina, as shown in column 24 lines 7-8 of the specification. The conditions to be controlled by Lamothe et al. are not identical to the conditions to be treated by the present application. Lamothe et al. never mentions "vaginitis and disturbance of the vaginal bacterial flora

or bacterial vaginosis accompanied with a reduction of the number of Gram-positive bacilli,” which are the conditions treated by the methods of the claims of the present application.

Furthermore, promoting the growth of Gram-positive bacilli *in vitro*, as described in Lamothe, et al. is not the same as being able to treat disturbance of vaginal flora or vaginitis or vaginosis. Even if one saccharide does promote the growth of Gram-positive bacilli *in vivo*, e.g., promote Gram-positive bacilli lactobacilli growth in the vagina, it is likely to fail to actually treat the disorders in the vagina. For example, lactose promoted the growth of Gram-positive bacilli lactobacilli *in vitro* as well as in the vagina of the patient as shown in Example 6 of the instant application, but it was not effective enough and failed to cure the abnormality of that patient.

It can be seen that the conditions to be treated in Lamothe et al. are not identical to these of the present application. Thus it is not expected for a person ordinary skill in the art to obtain the technical solution of the present invention and solve the problem pursued therein in view of Lamothe et al.

Furthermore, the composition of this invention combines sucrose/maltose with an anti-fungal agent. This combination shows an additive benefit for treating bacterial vaginal diseases as defined in the claims of this application and avoids the potential growth of yeast-like organisms. Experimental Examples 1 and 2 on pages 33-40 of the specification prove that the composition of this invention is capable of promoting the growth of vaginal lactobacilli while inhibiting the growth of *Candida*. It is quite unexpected to a person of ordinary skill in the art that a composition for treating bacterial vaginal diseases such as bacterial vaginosis may contain an anti-fungal agent. In the composition of the present invention, the anti-fungal agent that is to be vaginally used is not for treating fungal vaginitis when it is combined with sucrose/maltose. The composition of this invention and its use thereof was not previously known and is unpredictable to a person of ordinary skill in the art.

The history of culturing lactobacilli and producing fermented food is over hundreds of years old and the history of treating human beings suffering from bacterial infections including diseases of vagina is also over fifty years old. There are many institutions and pharmaceutical companies

committed to developing new drugs for treating bacterial infections of the vagina. However, no one else has discovered that sucrose and/or maltose alone or in combination with an anti-fungal agent can treat the reduced Gram-positive bacilli in the vagina and related disorders as defined in claim 11, and no one else has discovered that sucrose and/or maltose alone or in combination with an anti-fungal agent can cure vaginal microbial diseases. Bactericidal drugs and bacterial inhibitors are still the only choices for vaginal bacterial diseases. These facts confirm the unobviousness of this invention of using sucrose and/or maltose as the essential active ingredient to treat vaginal bacterial diseases. This medical use appears simple, but it goes against the general professional sense. The treatment result is unexpected and is a result of the inventor's extensively hard work.

Based on the foregoing, Applicants respectfully submit that the pending claims are not anticipated by Lamothe et al. nor are they rendered obvious by Lamonthe et al. Therefore, Applicants respectfully request reconsideration and withdrawal of the foregoing rejection.

**Rejection Under 35 U.S.C. §102(b) or 35 U.S.C. § 103(a) in view of Cohen et al.**

The Examiner has also rejected claims 1-4 and 6-13 under 35 U.S.C. §102(b) as being anticipated by Cohen et al. (U.S. Patent No. 6,165,997, referred to herein as the '917 patent), or, in the alternative, as being unpatentable over Cohen et al. under 35 U.S.C. §103(a). In particular, the Examiner states that the abstract of Cohen et al. discloses a pharmaceutical formulation for stimulating growth of Gram-positive Bacilli and increasing the acidity in the vagina comprising sucrose and/or maltose, optionally with other sugars, viscous base and anti-fungal agents. The Examiner is of the opinion that any differences in the amounts of the agents used would have been obvious to one of ordinary skill in the art at the time of the invention.

In making the present rejections, the Examiner has relied upon the abstract of the '997 patent. The Examiner has applied the '997 patent as prior art under 35 U.S.C. §102(b) based on the issue date of the '997 patent of December 26, 2000. Applicants respectfully submit that the present application has a priority date of May 24, 2000, which is prior to the issue date of the '997 patent. Thus, the '997 patent is not available as prior art under 35 U.S.C. §102(b). Furthermore, Applicants respectfully submit that the abstract printed on the face of the '997 patent is not entitled to the

claimed priority date of November 20, 1997, nor the filing date of November 19, 1998, and is therefore not available under any section of 35 U.S.C. §102, including 35 U.S.C. §102(e). The '997 patent was also cited in the parent application, now U.S. Patent No. 6,632,796. The following comments were also made by Applicants during prosecution of U.S. Patent No. 6,632,796.

The abstract of the '997 patent discloses a pharmaceutical formulation for stimulating growth of Gram-positive Bacilli and increasing the acidity in the vagina comprising sucrose and/or maltose and optionally additional components. No mention of the formulation is found in the specification of the '997 patent or in the claims of the '997 patent. The subject matter of the patent, excluding the abstract, is directed solely to the subject matter described in the title of the '997 patent, i.e., "Phospholipids having antimicrobial activity with or without the presence of antimicrobials." In short, the subject matter of the abstract bears no relation to the rest of the patent.

Applicants have obtained file wrappers of provisional application serial no. 60/066,901, filed on November 20, 1997 and the '997 patent. The transmittal papers submitted with the provisional application indicated submission of a specification of 29 pages, 0 sheets of drawings, and no claims. The 29 pages of the specification are present in the file wrapper of the provisional application. The abstract is not among them. In short, the abstract was not submitted as part of provisional application serial no. 60/066,901. Hence, the abstract is not available as prior art under 35 U.S.C. §102(e) based upon the filing of the provisional application.

Nor can a rejection under 35 U.S.C. §102(e) be established based on the filing date of the '997 patent. The transmittal papers submitted with the application that resulted in the '997 patent indicate submission of a specification of 43 pages, and executed declaration, a preliminary amendment, and an information sheet. The 43 pages of specification, beginning at the title page and ending through the claims, are present in the file wrapper of the '997 patent. They do not include the abstract that issued in the '997 patent. Nor is the abstract included in the preliminary amendment submitted with the application that resulted in the '997 patent, as filed. It is not printed on the information sheet submitted with the application. Hence, there is no evidence that the abstract was part of the application that resulted in the '997 patent, as filed. During prosecution of

the '997 patent, the Patent Office issued, *inter alia*, a Notice to File Missing Parts (Paper 2), an Office Action (Paper 10) and a Notice of Allowance (Paper 13). None of these papers requested submission of an abstract. The patentee filed a second Preliminary Amendment (Paper 4), and Amendment in response to the Office Action (Paper 12), and four Information Disclosure Statements (Papers 5, 6, 9, and 11). None of the papers submitted by the patentee included or referred to an abstract. In short, based on the papers of record in the file wrapper of the '997 patent, there is no evidence that the abstract appearing on the face of the patent was submitted or authorized by the patentee.

The abstract appearing on the face of the '997 patent is present in the file wrapper of the application that resulted in the '997 patent. However, in light of the foregoing discussion, the record fails to establish who placed the abstract in the file wrapper or when the abstract was placed in the file wrapper. There is therefore no basis to derive a date upon which the abstract would be available as prior art under 35 U.S.C. §102(e). Applicants therefore submit that the abstract of the '997 patent is not available as prior art under 35 U.S.C. §102(e). The abstract was available as a reference only upon issuance of the '997 patent on December 26, 2000. However, as set forth above, this date is after the filing date of the priority application of the present application, i.e., May 24, 2000. Thus '997 patent is not available as prior art against the present application under 35 U.S.C. §102(b).

In light of the foregoing discussion, Applicants respectfully request reconsideration and withdrawal of the instant rejection of the claims under 35 U.S.C. §102(b) or 35 U.S.C. §103(a).

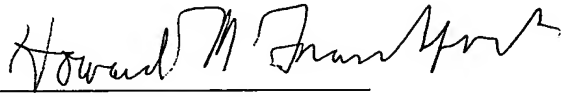
**Conclusion**

Claims 11-29 are in a condition for allowance.

In view of the above amendments and remarks, reconsideration of this application and issuance of a Notice of Allowance for claims 11-29 is earnestly solicited.

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Respectfully submitted,

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